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A VACCINE FOR THE TREATMENT OF BRONCHIAL ASTHMA: REPORT OF TWENTY CASES.¹

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THE work of Auer and Lewis, Meltzer, Vaughan, Babcock and others leaves little doubt that the disease so long known as bronchial or idiopathic asthma has been permanently removed etiologically from the neuroses, and is now fully explained as a manifestation of protein sensitization. The paroxysmal outbursts represent anaphylactic shock and the various causes formerly thought to act reflexly, and whose removal often resulted in cure, are now believed to be foci from which the foreign material necessary to induce an attack is elaborated.

Judging from the widely diversified nature of the exciting causes of asthmatic seizures it would seem probable that the specific poison either occurs in a number of forms or is common to a great variety of plants and animals as well as bacteria. Moreover, from our understanding of the conditions underlying sensitization it is evident that an immunity could be produced provided the specific protein was capable of being isolated in an available form and

¹ Read before the Nineteenth Annual Meeting of the Tri-State Medical Society, at Durham, N. C.

injected into the sensitized individual in suitable amounts and at proper intervals. This procedure, however, assuming that it was possible in more than a limited number of cases, would involve an amount of time and work far exceeding the means of the average sufferer from asthma.

Certain observations of the writers, derived from the study of a considerable number of cases of asthma, have strongly suggested the possibility of the presence of the specific protein in the bronchial secretions of the patient himself, and also that this protein may be recovered in suitable form for use in bringing about immunity.

In the fall of 1915 we began to prepare vaccines for asthma cases along the lines suggested by Babcock. From our first patient we succeeded in growing the organism described by him, along with a few streptococci and staphylococci. The result in this case was truly remarkable. The second or third injection was sufficient to give immediate and absolute relief for a period of a year. In our second attempt at sputum growth from an asthmatic we failed to grow Babcock's organism and despaired of making up the vaccine because of the fact we were led to believe from his results that his organism was specific for this condition. We did, however, prepare a vaccine from the growth which contained streptococcus, staphylococcus and *Micrococcus catarrhalis* along with a small amount of broth-culture media. The result in this case was even more striking than the first. Our third case was treated with the mixture of the broth sputum and the bacterial flora, and the outcome of the treatment was equally as startling. We then abandoned the anaërobic method of culture and commenced to grow our organisms by aërobic methods. More recently we have been adding a drop or two of guinea-pig serum along with the sputum and broth and incubating the whole for a period of forty-eight hours before making up our vaccine.

Our present vaccine is made in the following manner: 1 c.c. of washed sputum is incubated in 10 c.c. of broth and 1 or 2 drops of guinea-pig serum for a period of forty-eight hours. At the expiration of that time the culture is standardized and killed by heat of 60° C. for a period of two hours. Further decomposition is prevented by adding carbolic acid until a 1 per cent. solution results. This is cultured out to ensure sterility of our suspension. The vaccine is then diluted with normal saline until each cubic centimeter of the suspension contains 500,000,000 to 1,000,000,000 organisms. The initial dose is 5 minims and each subsequent dose is increased by 1 minim. We do not increase beyond 15 minims, although we may continue the treatment several weeks after this amount has been reached.

At first glance this mixture seems to be a gunshot one, but a more careful survey of its constituents and the results obtained by its administration should, in our opinion, warrant its use. It

is quite possible that the anaphylatoxin that is responsible for asthma may be produced *in vitro*, and that the proper administration of this anaphylatoxin may give a relative immunity to further intoxication.

Friedberger succeeded in producing toxic substances *in vitro*, and these gave rise to typical anaphylactic symptoms when injected into normal animals. In later experiments, however, he obtained similar poisons from bacteria and other proteins by their incubation with normal guinea-pig complement without the concurrence of a specific antibody; while other observers have been able to isolate similar poisons by the incubation of normal guinea-pig serum with starch, agar, etc., and have decided that the poison originated from the serum. Friedberger, however, objected to this on the grounds that the small amount of protein impurities in the agar and starch furnish the material for the formation of the anaphylatoxin.

The exact nature of asthma anaphylatoxin then is still unknown, but it is reasonable to believe that the anaphylactic symptoms are produced by the digestion and the split products of the sputum, bacteria, etc.

It has been observed that animals receiving injections of a foreign protein at short intervals develop a decided resistance to this substance, so that several lethal doses for a sensitized animal may be given without producing symptoms. If, however, the time between injections is sufficient to sensitize the animal anaphylactic shock will result. In other words, frequent doses at short intervals will confer an immunity to a protein, while if the dose is spaced over a period of eight to ten days the animal becomes hypersensitive. In giving vaccine we attempt to raise the resistance of our patients against the anaphylatoxin of asthma. In other words, we vaccinate against anaphylaxis, and the resulting state might be called anti-anaphylaxis.

We have been able so far to observe the effect of this plan of treatment in 20 cases of typical bronchial asthma.

In 12 of these cases complete relief from attacks was experienced after from one to five injections of the vaccine and this relief has persisted up to the present time. The longest period of freedom from symptoms is sixteen months, the shortest six weeks.

In 5 cases distinct improvement has been noted either in the frequency of the seizures, their severity, or their duration. In 3 of these cases improvement occurred only after a second vaccine had been made and administered at shorter intervals than the first.

In 2 cases no effect at all was produced. One of these patients was an elderly man with emphysematous lungs and a history of asthma extending over twenty years. Asthma in the other case had followed injury to the chest and roentgen-ray examination revealed ununited fractures of several ribs.

In 1 case administration of the vaccine seemed to increase the

intensity of the paroxysms, a result which appeared to be explained by the fact that too long a time was allowed to elapse between injections.

Injections have in most cases been made twice a week. We are of the opinion, however, that a shorter interval will prove more desirable. We have also attempted, in each case, to remove an obvious focus of infection, but have refrained from any other treatment while the vaccine was being used.

We have been greatly impressed by the above results and hope to determine in the near future (1) whether or not the elements constituting the mixture are effective if injected separately; (2) also which element is potent; (3) and whether the protein injected is specific or not.

A STUDY OF ATMOSPHERIC AIR IN THE UPPER DIGESTIVE TRACT.*

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It is only within recent years that sufficient attention has been accorded to the role played by atmospheric air in the physiology and pathology of the digestive tract. Although the symptoms associated with the presence of gas—belching, tympany, meteorism, flatulence, etc.—have been the subject of comment from the earliest times, it has most commonly been taken for granted that the gases in question have had their origin entirely within the body, whether from the decomposition of food, the exhalation of vapors or from the interplay of gas-producing juices. It would seem therefore advisable, before presenting any observations based on newer methods, to pass in brief review the more important of the many scattered observations of earlier writers.

I. HISTORICAL BACKGROUND.

Interest in the subject dates back to the time of Hippocrates, to whom is ascribed a book on the "winds" or "flatuosities."²¹ Following this authority, many of the ancients created an entity of the condition, to which they gave the name *morbus ructuosus*, and ascribed all sorts of disorders to it. These men became known as "pneumatists." This doctrine was energetically opposed by Combalusier (1747),¹¹ who attempted to give a more restricted significance to the role played by the gases.

* Read in part under the title of "The Physiology of Aerophagia," at a meeting of the Section on Medicine of the New York Academy of Medicine, December 18, 1917. Dr. Meltzer discussed the paper and his remarks are published in the Medical Record, 1918, xciii, 100.